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	L3	L1 and peptide	15
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> aminopeptidase (w) A

L1 1125 AMINOPEPTIDASE (W) A

=> inhibitor

L2 1384863 INHIBITOR

=> L1 and l2

L3 268 L1 AND L2

=> angiogenesis

L4 64888 ANGIOGENESIS

=> L1 and 14

L5 19 L1 AND L4

=> cancer and L3

L6 12 CANCER AND L3

=> diabetis and L1

L7 0 DIABETIS AND L1

=> diabitic (w) retinopathy

L8 0 DIABITIC (W) RETINOPATHY

=> retinopathy

L9 28419 RETINOPATHY

=> L1 and L9

L10 0 L1 AND L9

=> D L5 IBIB ABS 1-19

L5 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:291600 CAPLUS

**DOCUMENT NUMBER:** 

143:323403

TITLE:

Possible Involvement of Adipocyte-Derived Leucine

Aminopeptidase via Angiotensin II in Endometrial

Carcinoma

AUTHOR(S):

Shibata, Kiyosumi; Kikkawa, Fumitaka; Mizokami, Yayoi;

Kajiyama, Hiroaki; Ino, Kazuhiko; Nomura, Seiji;

Mizutani, Shigehiko

CORPORATE SOURCE:

Department of Obstetrics and Gynecology, Nagoya

University Graduate School of Medicine, Nagoya,

466-8550, Japan

SOURCE:

Tumor Biology (2005), 26(1), 9-16

CODEN: TUMBEA; ISSN: 1010-4283

PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: It has recently been appreciated that a local autocrine or paracrine renin-angiotensin system (RAS) may exist in a no. of tissues. Angiotensin II (AngII) is a potent RAS-derived vasoconstrictor peptide. and it is involved in tumor angiogenesis. We have cloned human adipocyte-derived leucine aminopeptidase (A-LAP), which degrades Ang II. This study investigated whether the expression of A-LAP, Ang II, angiotensin type I receptor (AT1R) and vascular endothelial growth factor (VEGF) correlates with clinicopathol. factors and prognosis in patients with endometrial endometrioid adenocarcinoma. Methods: Histol. sections of formalin-fixed, paraffin-embedded specimens from 94 primary endometrial carcinomas were stained for A-LAP, AngII, AT1R and VEGF using each antibody. Disease-free survival (DFS) and other clinicopathol. characteristics were analyzed according to the intensity of each staining. Results: Of 94 cases, 91 (96.8%) showed specific A-LAP immunostaining. A-LAP expression demonstrated neg. correlations with myometrial invasion (p = 0.01) and vascular infiltration (p = 0.01). Of 94 cases, 77 (81.9%) showed specific AngII immunostaining. We found a pos. correlation between AngII expression and surgical stage (p = 0.01). Of 94 cases, 56 (59.6%) showed specific AT1R immunostaining and 73 (77.7%) specific VEGF immunostaining. We found a pos. correlation between VEGF expression and lymph node metastasis (p = 0.05). AngII and AT1R expression predicted a significantly poorer prognosis. Contrarily, A-LAP expression indicated a significantly more favorable prognosis in endometrial endometrioid adenocarcinoma patients. Multivariate anal. demonstrated that A-LAP expression (odds ratio, 0.12; 95% confidence interval, 0.025-0.618; p = 0.01) was an independent prognostic factor. Conclusions: In this study, we demonstrated the existence of local RAS and A-LAP in endometrial endometrioid adenocarcinoma as prognostic predictors of clin. outcome. These findings suggest that the assessment of RAS and A-LAP status provides clin. useful prognostic information in patients with endometrial carcinoma.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:755284 CAPLUS

DOCUMENT NUMBER: 141:329327

TITLE: Regulatory role of membrane-bound peptidases in the

progression of gynecologic malignancies

AUTHOR(S): Ino, Kazuhiko; Shibata, Kiyosumi; Kajiyama, Hiroaki;

Kikkawa, Fumitaka; Mizutani, Shigehiko

CORPORATE SOURCE: Department of Obstetrics and Gynecology, Nagoya

University Graduate School of Medicine, Nagoya,

466-8550, Japan

SOURCE:

Biological Chemistry (2004), 385(8), 683-690

CODEN: BICHF3; ISSN: 1431-6730

PUBLISHER:

Walter de Gruyter GmbH & Co. KG

**DOCUMENT TYPE:** 

Journal; General Review

LANGUAGE:

English

AB A review. Membrane-bound peptidases play a key role in the control of growth, differentiation, and signal transduction of many cellular systems by degrading bioactive peptides. Thus, abnormal changes in their expression pattern and catalytic function result in altered peptide activation, which contributes to neoplastic transformation or progression. In this review, we describe our recent findings along with work from other groups on the expression and biol. functions of membrane-bound peptidases in cancer, focusing on the regulatory roles of three peptidases, aminopeptidase A (APA), neutral endopeptidase (NEP) and placental leucine aminopeptidase (P-LAP), in the progression of gynecol. malignancies. APA, NEP and P-LAP are differentially expressed and localized in various gynecol. malignancies including cervical cancer, endometrial cancer, ovarian cancer and choriocarcinoma in a tumor-type specific pattern. The expression levels are up- or down-regulated depending on histol. grade or disease progression. These peptidases play regulatory roles in tumor cell proliferation, invasion or angiogenesis via degrdn./inactivation of target peptides such as angiotensin II, endothelin-1 and oxytocin, which act on cancer cells as stimulatory or inhibitory factors. Thus, membrane-bound peptidases may become not only a new diagnostic/prognostic marker, but also a novel mol. target for the treatment of gynecol. malignancies.

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75 THERE ARE 75 CITED REFERENCES

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L5 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:483444 CAPLUS

**DOCUMENT NUMBER:** 

141:138044

TITLE:

Glutamyl-but not aspartyl-aminopeptidase activity is modified in serum of N-methyl nitrosourea-induced rat

mammary tumours

AUTHOR(S):

Carrera, Maria Pilar; Ramirez-Exposito, Maria Jesus;

Valenzuela, Maria Teresa; Garcia, Maria Jesus; Mayas,

Maria Dolores; Martinez-Martos, Jose Manuel

CORPORATE SOURCE:

Departamento de Ciencias de la Salud, Area de

Fisiologia, Universidad de Jaen, Jaen, Spain

SOURCE:

Anticancer Research (2004), 24(2B), 801-805

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER:

International Institute of Anticancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

AB The rat model of breast cancer induced by the administration of N-methyl-nitrosourea (NMU) constitutes a useful tool for dissecting the initiation, promotion and progression process of carcinogenesis. Angiogenesis, the recruitment of new blood vessels, is an essential component of the metastatic pathway. Tumor vessels have an aberrant response to constrictor hormones, such as angiotensin II (Ang II). Ang II degrdn. to form angiotensin III (Ang III) begins with the action of glutamyl aminopeptidase (GluAP) and aspartyl aminopeptidase (AspAP), named together as aminopeptidase A activity (APA). The present work analyses GluAP and AspAP activities in serum of NMU-induced rat mammary tumors, to evaluate the putative value of these activities as biol. markers of the initiation and promotion of the disease. Serum AspAP and GluAP activities were measured fluorimetrically using their corresponding aminoacyl-.beta.-naphthylamide. The increase found in GluAP but not in AspAP suggests an increase in Ang III and a decrease in Ang II serum circulating levels. Thus, the decrease in Ang II may be responsible for the overexpression of AT1 receptors described in breast cancer. However, increased levels of Ang III, which exhibit the same affinity for the AT1 receptor, would favor the development of the disease.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

**ACCESSION NUMBER:** 

2004:187472 CAPLUS

**DOCUMENT NUMBER:** 

140:233520

TITLE:

Aminopeptidase A is a functional

target in angiogenic blood vessels

AUTHOR(S):

Marchio, Serena; Lahdenranta, Johanna; Schlingemann,

Reinier O.; Valdembri, Donatella; Wesseling, Pieter; Arap, Marco A.; Hajitou, Amin; Ozawa, Michael G.; Trepel, Martin; Giordano, Ricardo J.; Nanus, David M.; Dijkman, Henri B. P. M.; Oosterwijk, Egbert; Sidman, Richard L.; Cooper, Max D.; Bussolino, Federico;

Pasqualini, Renata; Arap, Wadih

CORPORATE SOURCE: The University of Texas M.D. Anderson Cancer Center,

Houston, TX, 77030, USA

SOURCE:

Cancer Cell (2004), 5(2), 151-162

CODEN: CCAECI; ISSN: 1535-6108

PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We show that a membrane-assocd. protease, aminopeptidase

A (APA), is upregulated and enzymically active in blood vessels of human tumors. To gain mechanistic insight, we evaluated angiogenesis in APA null mice. We found that, although these mice develop normally, they fail to mount the expected angiogenic response to hypoxia or growth factors. We then isolated peptide inhibitors of APA from a peptide library and show that they specifically bind to and inhibit APA, suppress migration and proliferation of endothelial cells, inhibit angiogenesis, and home to tumor blood vessels. Finally, we successfully treated tumor-bearing mice with APA binding peptides or anti-APA blocking monoclonal antibodies. These data show that APA is a regulator of blood vessel formation, and can serve as a functional vascular target.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:1009865 CAPLUS

DOCUMENT NUMBER: 140:233409

TITLE: Adipocyte-Derived Leucine Aminopeptidase Suppresses

Angiogenesis in Human Endometrial Carcinoma

via Renin-Angiotensin System

AUTHOR(S): Watanabe, Yoshiteru; Shibata, Kiyosumi; Kikkawa,

Fumitaka; Kajiyama, Hiroaki; Ino, Kazuhiko; Hattori, Akira; Tsujimoto, Masafumi; Mizutani, Shigehiko

CORPORATE SOURCE: Department of Obstetrics and Gynecology, Nagova

Graduate University School of Medicine, Nagoya, Japan

SOURCE: Clinical Cancer Research (2003), 9(17), 6497-6503

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

AB Angiotensin (Ang) II was reported to induce vascular endothelial growth factor (VEGF) expression in various cells. Adipocyte-derived leucine aminopeptidase (A-LAP) is a novel member of the M1 family of zinc metallopeptidases. Enzymic characterization demonstrated that A-LAP hydrolyzes Ang II. This study examd. the role of A-LAP in angiogenesis of human endometrial carcinoma. Exptl. Design: We investigated whether Ang II induces VEGF expression in human endometrial carcinoma cells. To investigate the possible function of A-LAP in angiogenesis of endometrial carcinoma, we transfected A-LAP cDNA into HEC-1A cells, showing the lowest expression of A-LAP. In the present study, we showed that Ang II enhanced VEGF expression in a dose-dependent manner in endometrial carcinoma cells (HEC-1A cells). Overexpression of A-LAP attenuated Ang II-induced VEGF expression in HEC-1A cells. In addn., Human umbilical vascular endothelial cell migration was increased

in conditioned media from Ana II-treated wild-tune cells but not in

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Special Queries	#43 Searc	h STOCKER W and zinc endopeptidase	09:45:57	<u>22</u>
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	#1 Searc	h Ruiter D 1996	06:56:10	<u>29</u>

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